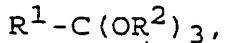


CLAIMS

1. A process for the resolution of enantiomeric mixtures of a chiral carboxylic acid of formula

5 R-COOH,

wherein R is a hydrocarbon residue optionally containing one or more heteroatoms and optionally mono- or polysubstituted, comprising an esterification reaction of said carboxylic acid in an organic solvent, in the presence of a 10 stereoselective hydrolase, characterized in that an orthoester of formula



in which  $R^1$  is selected from H and  $C_1-C_4$  alkyl and  $R^2$  is  $C_1-C_8$  alkyl or  $-CH_2-C_6-10$  aryl,

15 is used as the esterification reactive.

2. A process as claimed in claim 1, wherein  $R^1$  is selected from H, methyl, ethyl, n-propyl, n-butyl.

3. A process as claimed in claim 2, wherein said stereoselective hydrolase is a lipase selected from Candida antarctica, Candida cylindracea, Pseudomonas cepacia, Mucor miehei, Mucor javanicus, Aspergillus niger, swine pancreas, 20 or a protease from Aspergillus subtilis.

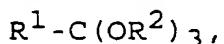
25 4. A process as claimed in any one of the above claims, wherein said esterification reaction is carried out at a temperature of 0-50°C, preferably at 45°C.

5. A process as claimed in any one of the above claims comprising the step of adding the reaction mixture with an amount of water or of a alcohol with 1-8 carbon atoms equivalent to 1-5% mols compared with the mols of said 30 chiral carboxylic acid.

6. A process as claimed in any one of the above claims, wherein in said esterification reaction the meso form of a bicarboxylic acid is used as substrate.

7. A process as claimed in the above claims 1-6, wherein said carboxylic acid is selected from  $(\pm)$  - (R,S) -2- (2-fluoro-4-biphenyl)-propionic,  $(\pm)$  - (R,S) -2- (3-benzoylphenyl)-propionic,  $(\pm)$  - (R,S) -2- (4-isobutylphenyl)-propionic,  $(\pm)$  - (R,S) -2- [4-(1-oxo-2-isoindolinyl)phenyl]propionic,  $(\pm)$  - (R,S) -2- [4-(2-thenoyl)phenyl]-propionic,  $(\pm)$  - (R,S) -2- (6-methoxy-2-naphthyl)-propionic acids.

8. The use of an orthoester of formula



10 in which R<sup>1</sup> is selected from H and C<sub>1</sub>-C<sub>4</sub>alkyl and R<sup>2</sup> is C<sub>1</sub>-C<sub>8</sub>alkyl or -CH<sub>2</sub>-C<sub>6</sub>-10aryl,  
in combination with a stereoselective hydrolase in the resolution of enantiomeric mixtures of carboxylic chiral acids.

15 9. The use as claimed in claim 8, wherein said hydrolase is a lipase selected from Candida antarctica, Candida cylindracea, Pseudomonas cepacia, Mucor miehei, Mucor javanicus, Aspergillus niger, swine pancreas, or a protease from Aspergillus subtilis.